

# ***Poly- L- lactic acid***

**Brand Name:** Sculptra

**Drug Class:** Opportunistic Infection and Other Drugs

## **Drug Description**

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Poly-L-lactic acid (PLLA) is a biocompatible, biodegradable, and immunologically inert synthetic polymer from the alpha-hydroxy-acid family. Microparticles of PLLA are the active ingredient in Sculptra, the injectable implant used for treatment of facial atrophy. [1] [2]

## **HIV/AIDS-Related Uses**

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PLLA was approved by the FDA on August 3, 2004, for the restoration and correction of the signs of facial fat loss in people with HIV.[3] Facial wasting is a common and disfiguring side effect of highly active antiretroviral therapy (HAART). Both nucleoside analogues and protease inhibitors are associated with the development of lipoatrophy.[4]

PLLA was approved in 1999 in Europe under the brand name New-Fill for the cosmetic treatment of wrinkles and has been used by an estimated 100,000 people. Dermik Laboratories, a Pennsylvania-based division of Sanofi-Aventis, filed with the FDA for premarket approval of PLLA in the United States under the brand name Sculptra.[5] On March 25, 2004, the FDA's General and Plastic Surgery Devices Advisory Panel recommended conditional approval for Sculptra for the treatment of HIV-associated lipoatrophy. Requirements for approval in the United States included a physician training program, a postmarket study enrolling women and people of color, clear labeling with warnings against off-label use, and a description of the product as having a reconstructive rather than a cosmetic purpose. Such strong labeling conditions are intended to greatly reduce the likelihood of adverse events reported in three previous U.S. trials and to discourage off-label use in HIV uninfected people.[6]

## **Non-HIV/AIDS-Related Uses**

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PLLA was approved in Europe in 1999 for the cosmetic correction of scars and wrinkles. PLLA is currently used in a variety of orthopedic and maxillofacial applications.[7]

## **Pharmacology**

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PLLA is the only treatment approved to correct sunken cheeks, hollow eyes, indentations, and other signs of facial fat loss, a common side effect of antiretroviral therapy for HIV. PLLA is injected into and around the deep dermis. The injections provide a gradual and significant increase in skin thickness, improving the appearance of folds and sunken areas.[8]

In a study of fifty HIV infected patients with severe facial atrophy, mean increases in facial total cutaneous thickness (TCT) of 6.8 mm were reported at Week 96, and 43% of patients had a facial TCT greater than 10 mm at Week 96. Patients in the study received three, four, or five sets of PLLA injections at 2-week intervals. One vial of reconstituted PLLA was injected into multiple points of each cheek per session. The number of sessions and the quantity of injected PLLA were dependent upon the severity of facial depression.[9]

A single-center study of PLLA was conducted in thirty HIV infected patients with facial lipoatrophy, and patients were followed for 12 or 24 weeks. All patients received three injection sessions conducted at 2-week intervals. All patients experienced statistically-significant increases in mean skin thickness compared with baseline. A mean increase in skin thickness of approximately 4 to 6 mm was observed in all patients at Week 12. In the fourteen patients observed for 24 weeks, mean increase in skin thickness was approximately 5 mm at Week 24.[10]

The progressive increase in dermal thickness may result from a local reaction followed by a progressive increase in collagen deposition. The bioactive material is degraded and safely undergoes resorption. Although PLLA injections are associated with an increase in TCT, there is no increase in subcutaneous fat.[11] For most people who participated in PLLA clinical studies, the treatment results lasted for up to 2 years after the first treatment session.[12]

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## **Adverse Events/Toxicity**

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PLLA injection has been associated with some adverse effects. In five clinical studies of HIV infected patients, no major adverse events were reported. Mild to moderate adverse events included bruising and hematoma related to injection.[13] The most common device-related adverse event was delayed occurrence of subcutaneous papules, which were confined to the injection site and were typically palpable, asymptomatic, and nonvisible.[14] Side effects reported at the March 25, 2004, meeting of the FDA General and Plastic Surgery Devices Advisory Panel included discomfort, bruising, edema, hematoma, inflammation, and erythema at the injection site. [15]

All patients had some degree of postinjection edema. A large proportion of patients (77%) experienced pain during the injection procedure, and about 28% of these patients required pain medication. About 13% of patients had postinjection noninflammatory nodules or papules. Severe side effects observed in limited clinical trials of PLLA included vagal hypertonia and lightheadedness (7.5%), inflammatory nodule development (1%), facial palsy upon hitting the facial nerve during treatment (1%), and anaphylaxis (1%).[16]

## **Drug and Food Interactions**

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No studies of interactions with PLLA with drugs or other substances or implants have been done.[17]

## **Contraindications**

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PLLA should not be used in any person who has hypersensitivity to any of the components of the product.[18]

## **Clinical Trials**

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For information on clinical trials that involve Poly-L-lactic acid, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Poly-L-lactic acid AND HIV Infections.

## **Dosing Information**

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Mode of Delivery: Deep dermis or subcutaneous (SQ) injection.[19]

Dosage Form: Clear glass vials containing freeze-dried preparation for injection sealed with a penetrable stopper and covered by an aluminum seal with a flip-off cap.[20] Sterile lyophilisate must be reconstituted with three ml of sterile water and should be injected using a 26-gauge needle.[21]

In clinical studies, patients have received three to five injection sessions at 2-week intervals. The dosage (quantity of injections and of sessions) depends upon the severity of facial depression.[22]

Storage: Store PLLA injection at room temperature, up to 30 C (86 F). Do not freeze.[23]

## **Chemistry**

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CAS Name: Propanoic acid, 2-hydroxy-, (S)-, homopolymer[24]

CAS Number: 26811-96-1[25]

Molecular formula: (C<sub>3</sub>H<sub>6</sub>O<sub>3</sub>)<sub>x</sub>[26]

Molecular weight: 40 to 50 kDa[27]

Stability: Each vial of PLLA for injection is packaged for single-use only; do not resterilize.[28]

PLLA is physically, chemically, and microbiologically stable for up to 72 hours after reconstitution, and for up to 2 years as a lyophilisate.[29] [30]

## **Other Names**

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PLA[31]

PLLA[32]

New-Fill[33]

## **Further Reading**

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## **Further Reading (cont.)**

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## **Manufacturer Information**

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Poly-L-lactic acid  
Dermik Laboratories, Inc.  
1050 Westlakes Dr.  
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(484) 595-2700

Sculptra  
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## **For More Information**

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Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help)  
Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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